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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/044,296	01/10/2002	Chris D. Constantinides	56783	6836

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EXAMINER	
CHAO, ELMER M	

ART UNIT	PAPER NUMBER
3737	

MAIL DATE	DELIVERY MODE
11/23/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/044,296	CONSTANTINIDES, CHRIS D.	
	Examiner	Art Unit	
	ELMER CHAO	3737	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-25,27 and 37-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6-25,27 and 37-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Acknowledgement is made of Applicant's amendment filed 7/15/2009 and Applicant's arguments filed 1/27/2009.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. **Claims 1-3, 6, 7, 9, 12-22, 24, and 37-42** are rejected under 35 U.S.C. 103(a) as being unpatentable over Judd et al. (U.S. 5,910,112) in view of Lauffer et al. (U.S. 5,628,982), further in view of Berg et al. (U.S. 5,128,121), and further in view of Foo (U.S. 2002/0087067).

Regarding **claims 1-3, 6, 7, 9, 12-15, and 37-39,** Judd '112 teaches a method of evaluating biological tissue by imaging it with ^{23}Na or ^{39}K magnetic resonance and a magnetic resonance system for ^{23}Na or ^{39}K MRI, where the tissue is cardiac tissue, where a study is made of the subject's heart and the cardiac tissue is identified as normal, injured or infarcted, where the subject has or had a cardiac or cardiovascular disorder, and manipulating echo time (TE) so as to assist in identifying infarcted myocardial tissue (C1, L15-18; C3, L32-37 & 46-53; C4, L12-30; C22, L43-67; C23, L1-23; C3, L2-5).

Judd '112 does not expressly teach the use of an iron oxide contrast agent so as to attenuate the ^{23}Na or ^{39}K MRI signal for ventricular cavity blood and viable well-perfused tissue. However, Berg '121 teaches a method of improving the contrast in MRI images by using a ferromagnetic or paramagnetic contrast agent such as an iron oxide bound to a polysaccharide (C2, L26-35) to decrease the signal level of the targeted tissue relative to its surroundings (C1, L10-38). It would have been obvious to a person having ordinary skill in the art to modify Judd '112 to include the use of iron oxide to attenuate the ^{23}Na or ^{39}K MRI signal for ventricular cavity blood and viable well-perfused tissue. Such a modification would enable an enhanced image contrast (C1, L10-26) so as to better distinguish viable and non-viable cardiac tissue, a criticality already established by Judd '112.

Judd '112 and Berg '121 do not expressly teach the use of the contrast before manipulating echo time. However, Lauffer '982 teaches adjusting imaging parameter values after the administration of the contrast agent (C25, L45-60). Therefore, it would have been obvious to a person having ordinary skill in the art to modify Judd '112 in view of Berg '121 to adjust the echo time after the administration of the contrast agent in order to accurately adjust for the diagnostic information sought (for motivation see C25, L45-60).

Judd '112, Berg '121, and Lauffer '982 do not explicitly teach providing a contrast between the ventricular cavity and infarcted myocardial tissue. However, in the field of myocardial infarction detection, Foo '067 teaches the method of providing a contrast between the ventricular cavity and infarcted tissue (Para [0036]). Therefore, it would

have been obvious to a person of ordinary skill in the art at the time of the invention to modify Judd '112, Berg '121, and Lauffer '982 to also provide contrast between the ventricular cavity and infarcted myocardial tissue in order to improve delineation of infarcted myocardium from ventricular blood pool and normal myocardium (for motivation see abstract; Para [0014]-[0015]).

Regarding **claims 16-22, 24, and 40,** Judd '112, Berg '121, Lauffer '982, and Foo '067 teach all of the limitations as discussed above. Judd '112, Berg '121, and Foo '067 do not explicitly teach manipulating the contrast agent. However Berg '121 does teach adjusting the contrast agent components and using an effective amount of the contrast agent so as to perform imaging to a particular contrast (col. 7, lines 12-46; col. 8, lines 23-48). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to have manipulated the contrast agent to reduce or increase the contrast to distinguish various tissues and blood pools in the heart (for motivation see Judd for identifying infracted tissue; also see Berg '121 for adjusting the contrast agent).

Regarding **claims 41 and 42**, Judd '112, Berg '121, Lauffer '982, and Foo '067 teach all of the limitations as discussed above. Judd '112, Berg '121, and Foo '067 do not explicitly teach manipulating the TE time to specifically reduce the ^{23}Na or ^{39}K MRI signals. However Judd '112 teach manipulating the TE (col. 6, line 66 – col. 7, line 27). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to have manipulated the TE in order to reduce the ^{23}Na or ^{39}K MRI signal in

ventricular cavity blood and viable well-perfused tissue (for motivation see Judd '112 col. 3, lines 46-65).

4. **Claims 8, 10-11, 23, 25, 27** are rejected under 35 U.S.C. 103(a) as being unpatentable over Judd '112 in view of Berg '121, further in view of Lauffer '982, further in view of Foo '067, further in view of Weissleder (U.S. 5,492,814). Judd '112, Berg '121, Lauffer '982, and Foo '067 teach all of the limitations as discussed above. Judd '112, Berg '121, Lauffer '982, and Foo '067 do not expressly teach the use of an iron oxide contrast agent with one or more iron atoms coordinated with a polymer having oxygen substitution, and with a dextran. However, Weissleder '814 teaches an iron oxide contrast agent for use in MRI, where the tissue imaged may be damaged heart tissue, such as infarcted myocardium, where the contrast agent has one or more iron atoms coordinated with a polymer having oxygen substitution, with a dextran and where the contrast agent is in a pharmaceutically acceptable form (C1, L16-24 & L41-55; C3, L1-11 & 28-36; C5, L7-16 & L50-63; C16, L61-67; C17, L1-12). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to have used the iron oxide contrast agent from Weissleder to enhance the visualization in the images of Judd '112 because the use of contrast agents in MRI to improve quality as previously shown by Berg '121, and further shown by Ranney (U.S. 5,336, 762) (C7, L48-61). Although neither Judd '112 nor Weissleder '814 nor Berg '121 nor Foo '067 specifically teach the use of MION-46, Weissleder '814 does teach the use of a variety

of MION formulas that include dextran, of which MION-46 would have been an obvious choice to one of ordinary skill in the art.

Response to Arguments

5. Applicant's arguments filed 1/27/2009 have been fully considered but they are not persuasive.

6. Regarding Applicant's arguments with respect to the Judd, Berg, Lauffer, Foo, and Weissleder references, Applicant points out that there is no teaching or suggestion to combine Judd with Berg, Lauffer, or Foo since Judd is directed towards increasing overall ^{23}Na and ^{39}K signals, whereas the instant application recites the attenuation of such signals in ventricular cavity blood and viable well-perfused tissue (page 8, paragraphs 2-4; page 9, paragraph 5; page 10, paragraph 3; page 11, paragraph 2; Arguments filed 1/27/2009). Examiner points out that Berg specifically teaches the method of using both positive and negative contrast agents such as iron oxide and targeting specific tissues, cavities, and/or blood pools (col. 2, lines 62-65; claim 2). Just because Berg doesn't point out specifically that the negative contrast agent is used to attenuate signals for ventricular cavity blood and viable well-perfused tissue does not mean that it would not be obvious to one of ordinary skill in the art to use Berg's attenuation methods for that particular application. The choice to amplify and attenuate specific types of tissues is a basic concept determined by the nature of the imaging being conducted and cannot be considered a non-obvious element in and of itself. One of ordinary skill in the art that wanted to image infarcted myocardial tissue would

immediately use the known method as suggested at least by Berg to attenuate tissues/blood pools not relevant to the infarcted myocardial tissue. Examiner also directs Applicant's attention to Arguments made in the Office Action filed 8/18/2008:

> " Regarding Applicant's arguments with respect to the Judd, Berg, and Foo references, Applicant also argues that Judd does not teach attenuating the MRI tissue for specific regions (page 10, paragraph 2, Arguments filed 7/23/2008). However, Examiner asserts that this modification would be obvious in view of the above-mentioned teachings of Judd and Berg. Judd's established criticality of imaging infarcted cardiac tissue in combination with using Berg's contrast agent(s) would provide enough for one of ordinary skill in the art to understand that contrast could be enhanced by attenuating the signals of the areas surrounding the infarcted cardiac tissue. Furthermore, Foo explicitly teach the method of providing a contrast between the ventricular cavity and infarcted tissue (Para [0036])."

7. Regarding Applicant's arguments with respect to the Judd, Lauffer, Berg, Foo, and Weissleder references, Applicant points out that Berg, Lauffer, Foo, and Weissleder do not pertain to ^{23}Na or ^{39}K MRI imaging in particular (page 8, paragraph 5 - page 9, paragraph 2; page 9, paragraph 5; page 10, paragraph 3; page 11, paragraph 2). However, Examiner disagrees because contrast agents, including iron oxide contrast agents are used commonly in MRI imaging. Judd teach ^{23}Na and ^{39}K imaging. Berg need not teach ^{23}Na and ^{39}K MRI imaging. One of ordinary skill in the art would

understand that using an iron oxide contrast agent as taught by Berg would help to enhance the contrast of the selected the infarcted cardiac tissue of Judd under the same type of ^{23}Na and ^{39}K imaging procedure that Judd already teaches.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ELMER CHAO whose telephone number is (571)272-0674. The examiner can normally be reached on Mon-Thurs 11am-9pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Casler can be reached on (571)272-4956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/BRIAN CASLER/
Supervisory Patent Examiner, Art Unit 3737

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